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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/843,342	04/25/2001	Bruce L. Roberts	GA0211US	8525

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GENZYME CORPORATION
LEGAL DEPARTMENT
15 PLEASANT ST CONNECTOR
FRAMINGHAM, MA 01701-9322

EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/843,342	ROBERTS ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2005 and 03 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 23-25* is/are pending in the application.

4a) Of the above claim(s) *1-6,12-21,23 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-11 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08252005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application claims the benefit of the filing date of provisional application 60/200,562.

Claim 22 has been canceled.

Claims 1-21 and 23-25 are currently pending.

Election/Restrictions

1. Claims **1-6, 12-21 and 23-24 stand as withdrawn pursuant to the Restriction Requirement mailed July 1, 2002.**

Claims **7-11 and 25 are the subject of examination** in the present Office Action.

In view of Applicant's amendment filed January 3, 2006 only the following outstanding grounds of rejection are maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 7-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites the limitation "the leucine zipper domain" in part (i). There is insufficient antecedent basis for this limitation in the claim. It is suggested that the recitations regarding the leucine zipper in parts (i) and (ii) in the claim be reversed.

Claim 11 is ambiguous and unclear in the recitation of a "recombinant system" in the preamble. There is insufficient nexus between elements (i) and (ii) of the claim to support the recitation as they also read upon separate components in a solution. Correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 7-11 and 25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,309,645 to Rhode et al. (A on form PTO-892) in view of U.S. Patent No. 5,932,448 to Tso et al. (B on form PTO-892), all of record.

It was previously stated: "The '645 patent teaches a polynucleotide comprising a nucleic acid molecule that encodes a soluble single chain MHC class II molecule with a covalently attached presenting peptide and a gene delivery vehicle comprising same (see entire patent; Abstract, Figures 24-30 in particular)[claims 7-8]. The '645 patent teaches host cells comprising the polynucleotide and the expressed polypeptide (Example 18 for example) [claims 9-10]. While the lexicography used in the '645 patent is different than that used in the instant specification, one of ordinary skill in the art would recognize the single chain MHC class II molecules of the '645 patent as satisfying the metes and bounds of the "T cell antigen presenting domain of an MHC molecule" as recited in the instant claims. The '645 patent further teaches a recombinant system comprising a first polynucleotide comprising a nucleic acid encoding a T cell antigen presenting domain of an MHC molecule (soluble single chain MHC class II molecule) and a second polynucleotide comprising a nucleic acid encoding a T cell epitope which binds specifically to the antigen presenting domain (presenting peptide; column 16, line 63 through column 17, line 10 in particular) [claims 11, 25]. The '645 patent teaches that homologous multivalent MHC fusion complexes are desirable for a number of applications. The '645 patent teaches, for example, that some T cells can only be stimulated by multivalent MHC complexes. The '645 patent teaches that multivalent MHC molecules can be made by fusing the single chain MHC molecules to immunoglobulin chains or recombinantly adding a reactive side chain amino acid residue to the C terminus to conjugate the single chain MHC molecules to a dendrimer (column 15, line 63 through column 16, line 27 in particular).

The '645 patent does not teach the use of leucine zippers to make homodimers of T cell antigen presenting domains of MHC molecules.

The '488 patent teaches nucleic acid molecules encoding a heavy chain portion of an Fab' immunoglobulin fragment attached to a leucine zipper domain. The '448 patent teaches that two Fab' fragments covalently attached to leucine zippers can be combined so that the leucine zippers will homodimerize to generate bispecific antibody constructs (see entire patent). The '448 patent teaches that Jun leucine zippers will readily form stable homodimers in the absence of Fos leucine zippers (column 5, lines 14-27 and column 5, line 49 through column 6, line 15 in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to genetically engineer the single chain T cell antigen presenting domain of an MHC molecule with or without a covalently attached presenting peptide as taught by the '645 patent as a fusion protein with the leucine zipper domain as taught by the '448 patent. One would have been motivated, with a reasonable expectation of success, to combine the teachings to make bivalent homodimers by the teaching of the '645 patent that multivalent molecules are desirable for stimulation of antigen-specific T cells and the teaching of the '448 patent that Jun leucine zippers will homodimerize in the absence of Fos leucine zippers and the dimers thus formed are efficient in forming dimers and are of high purity. One

would be further motivated to use the leucine zippers as taught by the '448 patent because the small size of the leucine zipper versus an immunoglobulin Fc region will result in a smaller recombinant complex and leucine zippers do not bear the immunogenic determinants of a xenogeneic immunoglobulin."

Applicant's arguments filed January 3, 2006 have been fully considered but they are not persuasive.

Applicant argues that the claimed invention is not obvious over the cited combination of references because the cited combination allegedly alters the principles of operation of the prior art and because there is a alleged lack of motivation to replace large immunoglobulin linkers with small leucine zipper linkers to create multivalent molecules because the molecules being joined would be seen by the artisan as being too large to be effectively joined using small linkers. Applicant argues that the cited combination of references allegedly teach away from the claimed invention.

Regarding the alleged lack of motivation to replace large linkers (immunoglobulin linkers of the '645 patent) with small leucine zipper linkers ('448 patent), Applicant's position is without merit. Applicant is reminded that the embodiment of the '645 patent embraced regarding MHC class II molecules is the single chain MHC class II molecules as depicted in Figures 24-30 for example. Applicant is arguing the use of the two-chain MHC class II molecules as depicted in Figure 1C, for example, which is considerably larger than the single chain molecule of figures 24-30. Indeed, the single chain MHC class II molecule including the linked immunogenic peptide, as depicted in Figure 30, is only 71 amino acids in length. This is smaller than the Fab fragments exemplified in Figures 2a-b of the '448 patent. Accordingly, there is no basis for the argument that the artisan would view the MHC class II single chain molecules of the '645 patent as being too large to join with leucine zipper homodimers whose units are 35 amino acid residues in length.

Regarding the contention the cited combination allegedly alters the principles of operation of the prior art; Applicant asserts that the Office "recognizes" this in the final sentence of the Office Action. The cited sentence states: "One would be further motivated to use the leucine zippers as taught by the '448 patent because the small size of the leucine zipper versus an immunoglobulin Fc region will result in a smaller recombinant complex and leucine zippers do not bear the immunogenic determinants of a xenogeneic immunoglobulin." Applicant's assertion is off point because, despite the fact that large linkers are exemplified in the '645 patent, there is no requirement in the '645 patent that the linkers be large. There is no teaching in the '645 patent to the effect that a smaller linker would not be effective. Fusing single chain MHC class II molecules to leucine zipper halves would yield a dimeric MHC class II construct. Dimeric constructs are clearly included within the scope of the '645 patent, as evidenced by Figure 2. Furthermore, changing away from an immunoglobulin linker to avoid xenogeneic antibody

responses as stated in the Office Action would by no means alter the principles of operation of the prior art as there is no teaching in the '645 patent that xenogeneic activity is an element of the invention. Furthermore, if the Fc region of the antibody were a required element in the '645 patent, the '645 patent could not have listed dendrimers or other linkers as preferred embodiments of the invention.

Accordingly, the finding of obviousness over the combined teachings of the '645 patent and the '448 patent is maintained.

Conclusion

4. No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. This application contains claims 1-6, 12-21 and 23-24 drawn to an invention nonelected without traverse in the Paper filed August 5, 2002. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D. FV
Patent Examiner
March 23, 2006

David A Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182 1644